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     (FILE 'HOME' ENTERED AT 09:13:30 ON 05 AUG 2003)

     FILE 'BIOSIS, MEDLINE, CAPLUS' ENTERED AT 09:13:56 ON 05 AUG 2003
L1             4 S IAP(10W)BIND? AND CELL CYCLE
L2             2 DUP REM L1 (2 DUPLICATES REMOVED)
L3           423 S IAP(10W)BIND?
L4           207 DUP REM L3 (216 DUPLICATES REMOVED)
L5           145 S IAP(10W)BIND? AND APOPTOSIS
L6            72 DUP REM L5 (73 DUPLICATES REMOVED)
L7           270 S SURVIVIN AND CELL CYCLE
L8           143 S SURVIVIN(15W)CELL CYCLE
L9            68 DUP REM L8 (75 DUPLICATES REMOVED)

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N 1999:26934 BIOSIS
DN PREV199900026934
TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.
AU Tamm, Ingo; Wang, Yan; Sausville, Ed; Scudiero, Dominic A.; Vigna, Nicole; Oltersdorf, Tilman; Reed, John C. (1)
CS (1) Burnham Inst., 10901 North Torrey Pines Road, La Jolla, CA 92037 USA
SO Cancer Research, (Dec. 1, 1998) Vol. 58, No. 23, pp. 5315-5320. ISSN: 0008-5472.
DT Article
LA English
AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell lines used for the National Cancer Institute's anticancer drug screening program. In cotransfection experiments, cell death induced by Bax or Fas (CD 95) was partially inhibited (mean +- SD, 65% +- 8%) by Survivin, whereas XIAP, another IAP family member, almost completely blocked cell death (93% +- 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP**-family proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using a cell-free system in which cytosolic extracts were derived from control- or Survivin-transfected cells and where caspases were activated either by addition of cytochrome c and dATP or by adding recombinant active caspase-8, Survivin was able to substantially reduce caspase activity, cleavage of a tetrapeptide substrate, AspGluValAsp-aminofluorocoumarin. Similar results were obtained in intact cells when Survivin was overexpressed by gene transfection and caspase activation was induced by the anticancer drug etoposide. Survivin was expressed in all 60 cancer cell lines analyzed, with highest levels in breast and lung cancers and lowest levels in renal cancers. These findings indicate that Survivin, which is commonly expressed in human tumor cell lines, can bind the effector cell death proteases caspase-3 and -7 in vitro and inhibits caspase activity and cell death in cells exposed to diverse apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.
TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.
AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell. . . almost completely blocked cell death (93% +- 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP**-family proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using. . . apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.
IT Major Concepts

CUS (LOC): MMCASP3 GenBank (R)
GenBank ACC. NO. (GBN): Y13086
GenBank VERSION (VER): Y13086.1 GI:2094809
CAS REGISTRY NO. (RN): 384754-53-4
SEQUENCE LENGTH (SQL): 1297
MOLECULE TYPE (CI): mRNA; linear
DIVISION CODE (CI): Rodents
DATE (DATE): 27 May 1997
DEFINITION (DEF): M.musculus mRNA for **caspase-3**.
SOURCE: house mouse.
ORGANISM (ORGN): Mus musculus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus
NUCLEIC ACID COUNT (NA): 380 a 255 c 314 g 348 t
REFERENCE: 1 (bases 1 to 1297)
AUTHOR (AU): Van de Craen,M.; Vandenabeele,P.; Declercq,W.; Van den Brande,I.; Van Loo,G.; Molemans,F.; Schotte,P.; Van Criekinge,W.; Fiers,W.
TITLE (TI): Characterization of seven murine caspase family members
JOURNAL (SO): FEBS Lett., 403 (1), 61-69 (1997)
OTHER SOURCE (OS): CA 126:235026
REFERENCE: 2 (bases 1 to 1297)
AUTHOR (AU): Van de Craen,M.
TITLE (TI): Direct Submission
JOURNAL (SO): Submitted (07-MAY-1997) M. Van de Craen, University of Gent, Laboratory of Molecular Biology, K.L. Ledeganckstraat 35, B-9000 Gent, BELGIUM

FEATURES (FEAT):

Feature Key	Location	Qualifier
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CDS	68..901	/standard-name="casp-3" /function="cysteine protease" /codon-start=1 /product="caspase-3" /protein-id="CAA73528.1" /db-xref="GI:2094810" /db-xref="SWISS-PROT:P70677" /translation="MENNKTSVDSKSINNFEVKT IHGSKSVDSGIYLDSSYKMDYPEM GICIIINNKNFHKSTGMSSRSGTDVDAANLRETF MGLKYQVRNKNDLTREDILELMDS VSKEDHSKRSSFVCVILSHGDEGVIYGTNGPVEL KKLTSFFRGDYCRSLTGKPKLFII QACRGTELDCGIETDSGTDEEMACQKIPVEADFL YAYSTAPGYYSWRNSKDGSWFIQS LCSMLKLYAHKLEFMHILTRVNRKVATEFESFSL DSTFHAKKQIPCIVSMLTKELYFY H"

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L5 A

4 ANSWER 72 OF 72 GENBANK.RTM. COPYRIGHT 2003 on STN

LOCUS (LOC): MMCASP7 GenBank (R)
GenBank ACC. NO. (GBN): Y13088
GenBank VERSION (VER): Y13088.1 GI:2094813
CAS REGISTRY NO. (RN): 190306-99-1
SEQUENCE LENGTH (SQL): 2372
MOLECULE TYPE (CI): mRNA; linear
DIVISION CODE (CI): Rodents
DATE (DATE): 27 May 1997
DEFINITION (DEF): M.musculus mRNA for **caspase-7**.
SOURCE: house mouse.
ORGANISM (ORGN): Mus musculus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus
NUCLEIC ACID COUNT (NA): 608 a 588 c 574 g 602 t
REFERENCE: 1 (bases 1 to 2372)
AUTHOR (AU): Van de Craen,M.; Vandenabeele,P.; Declercq,W.; Van den Brande,I.; Van Loo,G.; Molemans,F.; Schotte,P.; Van Criekinge,W.; Fiers,W.
TITLE (TI): Characterization of seven murine caspase family members
JOURNAL (SO): FEBS Lett., 403 (1), 61-69 (1997)
OTHER SOURCE (OS): CA 126:235026
REFERENCE: 2 (bases 1 to 2372)
AUTHOR (AU): Van de Craen,M.
TITLE (TI): Direct Submission
JOURNAL (SO): Submitted (07-MAY-1997) M. Van de Craen, University of Gent, Laboratory of Molecular Biology, K.L. Ledeganckstraat 35, B-9000 Gent, BELGIUM

FEATURES (FEAT):

Feature Key	Location	Qualifier
source	1..2372	/organism="Mus musculus" /strain="C3H/An" /db-xref="taxon:10090" /cell-line="L929r2" /cell-type="fibrosarcoma"
CDS	190..1101	/standard-name="casp-7" /function="cysteine protease" /codon-start=1 /product="caspase-7" /protein-id="CAA73530.1" /db-xref="GI:2094814" /db-xref="SWISS-PROT:P97864" /translation="MTDDQDCAAELEKVDSSSED GVDAKPDRSSIISSILLKKKRNAS AGPVRTGRDRVPTYLYRMDFQKMGKCIIINNKNF DKATGMDVRNGTDKDAGALFKCFQ NLGFEVTVHNDCSCAKMQDLLRKASEEDHSNSAC FACVLLSHGEEDLIYGKDGVTPIK DLTAHFRGDRCKTLLEKPKLFFIQACRGTELDDG IQADSGPINDIDANPRNKIPVEAD FLFAYSTVPGYYSWRNPGKGSWFVQALCSILNEH GKDLEIMQILTRVNDRVARHFESQ SDDPRFNEKKQIPCMVSMLTKELYFSR"

SEQUENCE (SEQ):
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=>

L6 ANSWER 33 OF 34 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:56316 CAPLUS
DN 130:278037
TI The **IAP family** of apoptotic regulators
AU Eiben, Lisa J.; Duckett, Colin S.
CS Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892-1578, USA
SO Results and Problems in Cell Differentiation (1998), 24(Apoptosis: Mechanisms and Role in Disease), 91-104
CODEN: RCLDAT; ISSN: 0080-1844
PB Springer-Verlag
DT Journal; General Review
LA English
AB A **review** with 54 refs. A perspective of the discovery and the evolution of our understanding of the inhibitor of **apoptosis** (IAP) proteins is presented. Structure and mechanism of action of vertebrate and invertebrate IAP proteins is discussed.
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
TI The **IAP family** of apoptotic regulators
AB A **review** with 54 refs. A perspective of the discovery and the evolution of our understanding of the inhibitor of **apoptosis** (IAP) proteins is presented. Structure and mechanism of action of vertebrate and invertebrate IAP proteins is discussed.
ST **review** IAP protein **apoptosis** regulation
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**IAP** (inhibitor of **apoptosis** protein); **IAP family** of apoptotic regulators)
IT **Apoptosis**
(**IAP family** of apoptotic regulators)

L6 ANSWER 34 OF 34 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1997:593613 CAPLUS
DN 127:245874
TI The iap genes: unique arbitrators of cell death
AU Clem, Rollie J.; Duckett, Colin S.
CS Dept of Molecular Microbiology and Immunology, The Johns Hopkins School of Hygiene and Public Health, Baltimore, MD, 21205, USA
SO Trends in Cell Biology (1997), 7(9), 337-339
CODEN: TCBIEK; ISSN: 0962-8924
PB Elsevier
DT Journal; General Review
LA English
AB A **review** with 18 refs. The **iap family** of anti-apoptotic genes, originally discovered in viruses, has grown considerably in the past two years with the addn. of a no. of evolutionarily conserved cellular homologs. Although the mechanism(s) by which these novel proteins block cell death is still unknown, intriguing clues to their function have been revealed by the discovery of interactions between some of the IAP homologs and cellular proteins involved in carrying out apoptotic signaling. Here, Rollie Clem and Colin Duckett discuss how the various IAP proteins may function in regulating **apoptosis**.
AB A **review** with 18 refs. The **iap family** of anti-apoptotic genes, originally discovered in viruses, has grown considerably in the past two years with the addn. of a no. of evolutionarily conserved cellular homologs. Although the mechanism(s) by which these novel proteins block cell death is still unknown, intriguing clues to their function have been revealed by the discovery of

interactions between some of the IAP homologs and cellular proteins involved in carrying out apoptotic signaling. Here, Rollie Clem and Colin Duckett discuss how the various IAP proteins may function in regulating **apoptosis**.

ST **review** iap gene **apoptosis**

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(IAP (inhibitor of **apoptosis**); iap genes and IAP proteins in **apoptosis**)

IT **Apoptosis**
(iap genes and IAP proteins in **apoptosis**)

IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(iap; iap genes and IAP proteins in **apoptosis**)

=>

L9 ANSWER 68 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 40
AN 1999:27863 BIOSIS
DN PREV199900027863
TI Control of apoptosis and mitotic spindle checkpoint by survivin.
AU Li, Fengzhi; Ambrosini, Grazia; Chu, Emily Y.; Plescia, Janet; Tognin, Simona; Marchisio, Pier Carlo; Altieri, Dario C. (1)
CS (1) Boyer Cent. Mol. Med., Dep. Pathol., Yale Univ. Sch. Med., 295 Congress Ave., New Haven, CT 06536 USA
SO Nature (London), (Dec. 10, 1998) Vol. 396, No. 6711, pp. 580-584. ISSN: 0028-0836.
DT Article
LA English
AB Progression of the cell cycle and control of apoptosis (programmed cell death) are thought to be intimately linked processes, acting to preserve homeostasis and developmental morphogenesis. Although proteins that regulate apoptosis have been implicated in restraining cell-cycle entry and controlling ploidy (chromosome number), the effector molecules at the interface between cell proliferation and cell survival have remained elusive. Here we show that a new inhibitor of apoptosis (IAP) protein, **survivin**, is expressed in the G2/M phase of the **cell cycle** in a cycle-regulated manner. At the beginning of mitosis, survivin associates with microtubules of the mitotic spindle in a specific and saturable reaction that is regulated by microtubule dynamics. Disruption of survivin-microtubule interactions results in loss of survivin's anti-apoptosis function and increased caspase-3 activity, a mechanism involved in cell death, during mitosis. These results indicate that survivin may counteract a default induction of apoptosis in G2/M phase. The overexpression of survivin in cancer may overcome this apoptotic checkpoint and favour aberrant progression of transformed cells through mitosis.
AB. . . between cell proliferation and cell survival have remained elusive. Here we show that a new inhibitor of apoptosis (IAP) protein, **survivin**, is expressed in the G2/M phase of the **cell cycle** in a cycle-regulated manner. At the beginning of mitosis, survivin associates with microtubules of the mitotic spindle in a specific. . .

=>

ANSWER 1 OF 251 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:206849 BIOSIS
DN PREV200300206849
TI Mammalian **IAP** gene **family**, primers, probes and detection methods.
AU Korneluk, Robert G. (1); MacKenzie, Alexander E.; Baird, Stephen; Liston, Peter
CS (1) Ottawa, Canada Canada
ASSIGNEE: Aegera Therapeutics Inc., Verdun, Canada
PI US 6541457 April 01, 2003
SO Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 1 2003) Vol. 1269, No. 1, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133.
DT Patent
LA English
AB Disclosed is substantially pure DNA encoding mammalian IAP polypeptides; substantially pure polypeptides; and methods of using such DNA to express the IAP polypeptides in cells and animals to inhibit **apoptosis**. Also disclosed are conserved regions characteristic of the **IAP-family** and primers and probes for the identification and isolation of additional IAP genes. In addition, methods for treating diseases and disorders involving **apoptosis** are provided.

L3 ANSWER 9 OF 251 CAPLUS COPYRIGH

N 1999:26934 BIOSIS
DN PREV199900026934
TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.
AU Tamm, Ingo; Wang, Yan; Sausville, Ed; Scudiero, Dominic A.; Vigna, Nicole; Oltersdorf, Tilman; Reed, John C. (1)
CS (1) Burnham Inst., 10901 North Torrey Pines Road, La Jolla, CA 92037 USA
SO Cancer Research, (Dec. 1, 1998) Vol. 58, No. 23, pp. 5315-5320. ISSN: 0008-5472.
DT Article
LA English
AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell lines used for the National Cancer Institute's anticancer drug screening program. In cotransfection experiments, cell death induced by Bax or Fas (CD 95) was partially inhibited (mean +- SD, 65% +- 8%) by Survivin, whereas XIAP, another IAP family member, almost completely blocked cell death (93% +- 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP**-family proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using a cell-free system in which cytosolic extracts were derived from control- or Survivin-transfected cells and where caspases were activated either by addition of cytochrome c and dATP or by adding recombinant active caspase-8, Survivin was able to substantially reduce caspase activity, cleavage of a tetrapeptide substrate, AspGluValAsp-aminofluorocoumarin. Similar results were obtained in intact cells when Survivin was overexpressed by gene transfection and caspase activation was induced by the anticancer drug etoposide. Survivin was expressed in all 60 cancer cell lines analyzed, with highest levels in breast and lung cancers and lowest levels in renal cancers. These findings indicate that Survivin, which is commonly expressed in human tumor cell lines, can bind the effector cell death proteases caspase-3 and -7 in vitro and inhibits caspase activity and cell death in cells exposed to diverse apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.
TI IAP-family protein survivin inhibits caspase activity and **apoptosis** induced by Fas (CD95), bax, caspases, and anticancer drugs.
AB Survivin is a member of the inhibitor of **apoptosis** protein (IAP) family. We investigated the antiapoptotic mechanism of Survivin, as well as its expression in 60 human tumor cell. . . almost completely blocked cell death (93% +- 4%) under the same conditions. Survivin and XIAP also protected 293 cells from **apoptosis** induced by overexpression of procaspase-3 and -7 and inhibited the processing of these zymogens into active caspases. In vitro binding experiments indicated that, like other **IAP**-family proteins, survivin **binds** specifically to the terminal effector cell death proteases, caspase-3 and -7, but not to the proximal initiator protease caspase-8. Using. . . apoptotic stimuli. Although quantitative differences may exist, these observations suggest commonality in the mechanisms used by IAP-family proteins to suppress **apoptosis**.
IT Major Concepts